REMARKS/ARGUMENTS

Claims 1, 3, 4, 6-11 and 33-35 are active. Claims 2, 5, and 12-32 have been withdrawn from consideration. Claim 1 has been amended to refer to specific mucoadhesive polymers previously described in claim 6 or on page 12 of the specification and to refer to an inner matrix "consisting essentially of a mucoadhesive polymer having a mucoadhesive effect". Claim 1 has been revised to eliminate redundant language, such as the phrases referring to optional components and parts a) and b) which optional components are encompassed by the revised language. Claim 6 has been amended to refer to the elected species. New claim 33 finds inherent support in the Examples which disclose compositions not containing gelatin. New Claims 34 and 35 find support in the original claims, especially claim 1. Claim 35 refers to the elected species. Accordingly, the Applicants do not believe that any new matter has been incorporated. Favorable consideration of this amendment and allowance of this application are respectfully requested.

Restriction/Lack of Unity/Election of Species

The Applicants previously elected with traverse **Group I**, claims 1-18 and 20-30, directed to an oral multiparticulate composition, and the species **centrorelix (active substance), anionic (meth)acrylate copolymers (EUDRAGIT) L type (outer coating), absence of separating layer, and absence of biophilic matrix**. The requirement has been made FINAL. The Applicants understand that additional species will be rejoined and examined upon an indication of allowability for a generic claim reading on the elected species. The Applicants respectfully request that the claims of the nonelected group which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04. Claim 5 has been amended for clarity and to address the Examiner's objection to it.

Provisional Rejection--Obviousness-type Double Patenting

Claims 1, 3, 4, and 6-11 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1-5 and 17-19 of copending U.S. Application No. 12/030,377. The Applicants respectfully request that this provisional double patenting rejection be held in abeyance pending the identification of otherwise allowable subject matter in the present application. Upon an indication of allowability for the pending claims, the Applicants understand that the provisional double patenting rejection will be withdrawn, provided the claims in the copending application have not been allowed, MPEP 804(I)(B).

Rejection—35 U.S.C. §112, first paragraph

Claim 10 was rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. The Applicants respectfully traverse this rejection, since claim 10 is an original claim and forms part of the original disclosure. Moreover, this claim finds descriptive support at the top of page 9 of the specification. Clearly, the concept of incorporating the active substances described in this claim was possessed by the Applicants as of their filing date. Actual exemplification is not required to meet the description requirement, see MPEP 2163 (I). Accordingly, this rejection may now be withdrawn.

Rejection—35 U.S.C. §112, first paragraph

Claims 1, 3, 4, 6-9, and 11 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. The Applicants respectfully traverse this rejection,

since these claims are original claims and form part of the original disclosure. Moreover, examination has been restricted to the elected species and no rejection of the elected species for lack of adequate description has been made. With respect to "a peptide or a protein, including derivatives or conjugates thereof" these are generically claimed and would be recognized by those of skill in the art as peptides, proteins and their derivatives and conjugates have well-known structural features. Accordingly, this rejection may now be withdrawn.

Rejection—35 U.S.C. §112, second paragraph

Claims 1, 3, 4, and 6-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendments above.

Rejection—35 U.S.C. §112, second paragraph

Claims 1, 3, 4, and 6-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendments above.

Rejections—35 U.S.C. §112, second paragraph

Claims 9-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. These rejections are moot in view of the amendments above. The term "Da" now appearing in claim 9 finds support on page 9, line 35 and the term "abarelix" appearing in claim 10 on page 8, last line.

Mucoadhesive vs. Bioadhesive

The present invention stands for targeted release of a mucoadhesive formulated active ingredient. Chitosan is one such mucoadhesive component and in the invention it is

formulated to exhibit mucoadhesive properties, that is, to specifically bind to the intestinal mucosa and release the active substance there (see the top of page 5 of the specification). As required by claim 1 the "mucoadhesive matrix layer is exposed and binds to the intestinal mucosa and releases the active substance there".

On the other hand, the prior art composition of Watts et al., U. S. Patent No 6,464,626, while containing chitosan, also contains a substantial amount of gelatin—a bioadhesive component that preferentially binds to glycocalyx on a cellular membrane instead of mucus. New claim 33 explicitly excludes gelatin and independent claim 1 requires release of the active substance when the "mucoadhesive matrix layer is exposed and binds to the intestinal mucosa and releases the active substance there". The Watts composition contains a high percentage of gelatin (see Examples 1-4 which incorporate 86.7%, 77.12%, 59.9% and 79.9% gelatin) and would exhibit bioadhesive effects which are disadvantageous compared to the mucoadhesive binding of the invention. The Watts compositions do not specifically target the active ingredient for mucosal release.

Since gelatin is the main component in the mixtures of Watts et al., the compositions of Watts et al. will bind in first place to the glycocalyx membrane. This type of binding is called "bioadhesive" in contrast to "mucoadhaesive". "Bioadhesive" means binding to the glycocalyx membrane but not to the mucus. This has the disadvantage that the particles are stuck or glued to glycocalyx of the intestine cells. This is undesirable because binding to the glycocalyx may cause irritation of the cells and unwanted pharmacological side effects. Moreover, the addition of gelatin at least diminishes the beneficial effects of mucosal binding by chitosan and mucosal release of the active substance since the glycocalyx will be covered by gelatin complexes.

The present invention avoids such disadvantageous effects since mucosal-targeted complexes bound to the mucus will be washed away after the release of the active ingredient

by the natural, on-going, renewal of the mucus layer. Further description of bioadhesive binding of gelatin to glycocalyx membrane is provided by WO 93/13753 at page 28, line 33-page 29, line 2 and at page 13, lines 14-23 and Fig. 3.

Rejection—35 U.S.C. §103(a)

Claims 1, 3, 6, 7, 8, 10 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Watts, et al., U.S. Patent No 6,465,626. The Applicants respectfully submit that this rejection would not apply to the present claims since Watts does not disclose or suggest a matrix consisting essentially of a mucoadhesive polymer. Rather, as explained above, the Watts compositions contain a substantial amount of a bioadhesive component such as gelatin that would bind to the glycocalyx of the cell membrane and thus not target active ingredient release to the mucosa. Watts also does not suggest selecting a polymer exhibiting "a mucoadhesive effect of η_b = 150 to 1000 mPa·s and a water uptake of from 10 to 750% in 15 min in a range of +/- 0.5 pH units relative to the pH at which the outer coating starts to dissolve". Moreover, this rejection would not apply to new claim 33 which excludes gelatin from the inner matrix. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §103(a)

Claims 1 and 4 were rejected under 35 U.S.C. §103(a) as being unpatentable over Watts, et al., U.S. Patent No 6,465,626, as applied to claims 1, 3, 6, 7, 8, 10 and 11, and further in view of Berliner, et al., U.S. Patent No. 5,849,327. Watts has been addressed above and does not disclose an inner matrix consisting essentially of a mucoadhesive polymer that targets release of the active component to the mucosa. Berliner was cited as a secondary reference teaching coating thickness, however, it also does not disclose or suggest

the mucoadhesive inner matrix of the invention. Accordingly, this rejection may now also be withdrawn.

Rejection—35 U.S.C. §103(a)

Claims 1, 9 and 10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Watts, et al., U.S. Patent No 6,465,626, as applied to claims 1, 3, 6, 7, 8, 10 and 11, and further in view of Engel, et al., U.S. Patent No. 5,773,032. Watts has been addressed above and does not disclose an inner matrix consisting essentially of a mucoadhesive polymer that targets release of the active component to the mucosa. Engel was cited as a tertiary reference teaching the active ingredient centrorelix, however, it also does not disclose or suggest the other elements of the invention such as a mucoadhesive inner matrix. Moreover, none of the prior art suggests or provides a reasonable expectation of success that centrorelix would be compatible with the other components of the invention and be released as required by claim 1. Accordingly, this rejection may now also be withdrawn.

Conclusion

In view of the amendments and remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

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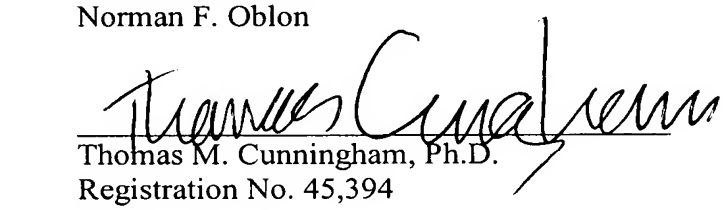

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